Short Report: Human Ocular Infection with *Dirofilaria repens* (Railliet and Henry, 1911) in an Area Endemic for Canine Dirofilariasis

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Abstract. *Dirofilaria repens*, which is usually found in canine subcutaneous tissues, is the main causative agent of human dirofilariasis in the Old World. However, a relationship between animal and human cases of dirofilariasis caused by *D. repens* in a given area has never been demonstrated. The uneven distribution of *D. repens* in provinces in Sicily, Italy represented the foundation for this study. We report a human case of ocular infection with *D. repens* from Trapani Province, where canine dirofilariasis is endemic. The nematode was morphologically and molecularly identified and surgical removal of the parasite was documented. The relationship between the prevalence of *D. repens* in dogs and the occurrence of human cases of ocular dirofilariasis is discussed on the basis of a review of the historical literature.

Zoonotic filarioids are transmitted at larval stage by blood- 
sucking insects from infected animals to humans. Among 
several species of filarial worms, human infections are mostly 
caused by nematodes belonging to the genus *Dirofilaria* 
(Spirurida, Onchocercidae), which are located predominantly 
in the subcutaneous tissues and pulmonary vessels, but also in 
central nervous system, and cause a range of clinical mani-
festations from asymptomatic to more severe (e.g., cough, chest 
pains, eosinophilia, and hemoptysis). Although *Dirofilaria immitis*, the agent of cardio-pulmonary disease in dogs is consi-
dered with the filarioid of raccoons (*Dirofilaria tenuis*) the 
main agent of human dirofilariasis in the Americas, *Dirofilaria repens*, which is usually found in the subcutaneous tissue 
of dogs, is the main causative agent of human dirofilariasis in 
the Old World. In most human cases of ocular dirofilariasis caused by *D. repens*, the parasites have been found in nodules or cysts 
in eye or in periocular tissues.

Identification of nematodes at species level relies on micro-
scopic examination of key characteristics (e.g., morphology of 
the body wall). A recent re-examination of 28 cases of human 
dirofilariasis reported in the past 30 years in the Old Word 
and erroneously attributed to *D. immitis* or *Dirofilaria* species 
other than *D. repens* indicated that *D. repens* was the prevalent 
species causing human infection. The DNA barcoding of *cox* 
and 12S mitochondrial markers has been shown to be useful 
for taxonomic identification of many filarial species. This 
approach, coupled with morphologic identification, enabled us 
to describe the first case of human intraocular infection with 
*Onchocerca lupi* in Turkey. In spite of its reduced pathogenic-
ity for dogs, *D. repens* is the species most frequently 
identified in human cases and it has been recently considered as an 
emerging metazoonosis in southern Europe. Although the 
relationship between animal and human cases of dirofilari-
asis in a given area could be expected, the correlation between 
infection rate in dogs and in humans has not been clearly 
documented.

A large survey was carried out on 2,512 dogs in nine prov-
inces in Sicily, Italy to estimate the prevalence of microfil-
aremia of different filarial species (Giannetto S and others, 
unpublished data). In this study, although *Acanthocheilonema reconditum* infection was detected in dogs from all the prov-
ces sampled, a significantly higher prevalence of *D. repens* 
(30.8%) was found in animals in Trapani Province than in those 
from other provinces (0.4–4.7%). The uneven distribution of *D. repens* in provinces in Sicily represented the foundation for the present work. We report a human case of ocular infection with *D. repens* in Trapani, an area to which canine dirofilariasis is endemic. The relationship between microfilaricemic dogs and human cases of dirofilariasis by *D. repens* is also discussed on the basis of a review of the historical literature.

A 55-year-old man came to the Ospedale Riccardo Guzzardi 
Vittoria (Ragusa, Sicily) with intense pain and redness in the 
right eye. The patient reported eyelid swelling in the right eye, 
photophobia, conjunctiva irritation, and a history of painful 
insect bites on his forehead, five months earlier, at the begin-
ning of summer (June) during a trip to Trapani.

Ophthalmologic examination showed a nematode under the 
bulbar conjunctiva of the right eye of the patient, and 
surgery for the removal of the nematode was recommended. 
After topical anesthesia, the palpebral fissure was kept open 
by using a blefarostat, and the nematode was gently extracted 
after incision of the conjunctiva membranes (Figure 1 and 
Supplemental Video). The patient recovered without compli-
cations within two weeks after surgery.

After extraction, the nematode was morphologically stud-
ied by using light microscopy and scanning electron micros-
copy. A small section (approximately 3 mm) of the nematode 
was used for DNA extraction and subsequent amplification 
of *cox*1 gene fragments as described. After identification, the 
parasite was deposited at the Muséum National d’Histoire 
Naturelle, Parasitologie Comparée, Paris, France (MNHM 
accession no. 194 YU).

The parasite was a female *Dirofilaria* sp. that had a length 
of 117 mm and minimum and maximum widths of 170 μm and 
530 μm (at the anus and vulva, respectively). The narrow 
hypodermal lateral chords were typical of *Dirofilaria* spp. In addition, scanning electron microscopy showed external cuticular ridges 7–12 μm apart, which are typical of *D. repens* (Figure 2). Other measurements were within the range of those for *D. repens* (length of the esophagus = 1,055 μm, a nerve ring 
260 μm from the anterior edge, and the anus 120 μm from the 
posterior edge). In accordance with morphologic identification, 
BLAST analysis (http://blast.ncbi.nlm.nih.gov/Blast.cgi) of the 
*cox*1 gene was identical with those of *D. repens* genes available in GenBank (accession nos. AM749234 and AM749232).
This case of ocular dirofilariasis was caused by *D. repens*. Anamnesis showed that the patient probably acquired the parasite in Trapani Province. Interestingly, as for previous cases of human ocular dirofilariasis caused by *D. repens*, the patient recollected a particularly painful insect bite, but it was impossible to say what insect was involved and whether the infection was transmitted at that time. In contrast to some human cases of dirofilariasis, no dermatologic signs (e.g., dermo-epidermal eruptive patches and itch) were recorded in the case reported herein. Cutaneous symptoms in human dirofilariasis has been attributed to the nematode tissue migration phase or, less frequently, by microfilariae in capillary vessels. The lack of dermatologic signs in our case might be explained by the absence of both events. Since the first reported case of nematode infection in the human eye as *Filaria conjunctivae*, *D. repens* has been implicated as the predominant causative agent of ocular dirofilariasis throughout the Old World. Most of the 492 cases reported in Europe have been in Italy (n = 117) and, in particular, from Sicily. However, these numbers are likely underestimated because of the lack of accurate etiologic diagnoses and because some cases are likely to go unreported in the literature.

The role of dogs as reservoirs of *D. repens* or the strict relationship between canine subcutaneous infection in a given area and human cases of dirofilariasis by *D. repens* have not been fully demonstrated. The patient in this study was likely infected with *D. repens* in Trapani Province, an area to which canine dirofilariasis is endemic and which has a prevalence of microfilaramic dogs up to 30.8% (Giannetto S and others, unpublished data). Accordingly, by reviewing the scientific literature on ocular dirofilariasis in Italy from 1866 through 2000, of the 14 patients in Sicily with ocular dirofilariasis, eight were from Trapani Province. The distribution of human dirofilariasis in Sicily overlaps the prevalence of *D. repens* infection observed by Giannetto and others (unpublished data) in dogs in the same provinces of Sicily (Figure 3). However, the role of dogs as reservoirs and transmitters (by mosquito bites) of human dirofilariasis and the correlation between infection rate in dogs and in humans should be further investigated by considering other factors that could affect the distribution of this human infection in a given area (e.g., species of mosquitoes, competent vectors).

Similarly, the first case of human intraocular dirofilariasis by a *Dirofilaria* sp. closely related to *D. immitis* has recently been reported from Brazil in a region where canine dirofilariasis by *D. immitis* is endemic; prevalence of microfilaramic dogs up to 32.45%. A relationship between human dirofilariasis and endemicity of *D. immitis* in dog populations has been suggested in some areas of the United States and Brazil. Dogs represent a good source of *D. immitis* and *D. repens* for mosquitoes because these dogs remain microfilaremic for several months to more than three years, and female worms in these dogs produce up to 5,000 microfilariae/day.

![Figure 1](image1.png)  
**Figure 1.** Human ocular dirofilariasis caused by *Dirofilaria repens*. Surgical removal of the nematode from the patient’s conjunctiva. A, incision of the bulbar conjunctiva cyst; B, the worm, in coiled shape, is clearly visible after the conjunctiva incision; C, *D. repens* emerging spontaneously from the conjunctiva cyst; D, the empty cyst remaining after nematode extraction.

![Figure 2](image2.png)  
**Figure 2.** Scanning electron microscopy of external cuticular ridges of *Dirofilaria repens* (bar = 20 μm).
Thus, introduction and spread of *Aedes albopictus* in some countries in Europe, including southern Italy, increased the risk of human dirofilariasis transmission. A. albopictus is well established throughout regions where *D. repens* is endemic and has been demonstrated to be a competent vector of *D. immitis* and *D. repens*.

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Note: The supplemental video appears at www.ajtmh.org.

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